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Att'y Dkt. No.: CONN001

USSN: 09/780,752

MAR 05 2003

I. AMENDMENTS

TECH CENTER 1600/2900

I.A. AMENDMENTS TO THE SPECIFICATION

On page 5, please enter the amendments to the paragraph beginning on line 14, as follows:

Q1 Figures 3A-D are graphs depicting the effect of a 5-day infusion of either rhRLX (4 µg/hour) or vehicle (time-control) on mean arterial pressure (MAP) MAP (panel A), glomerular filtration rate (GFR) GFR (B), effective renal plasma flow (ERPF) ERPF (C) or renal vascular resistance (ERVR) ERVR (D) in conscious male rats. * p < 0.05 vs baseline.

On page 5, please enter the amendment to the paragraph beginning on line 21, as follows:

Q2 Figure 5 is a graph depicting real-time quantitative reverse transcription-polymerase chain reaction (RT-PCR) RT-PCR analysis of expression of the rat VEGF₁₆₄ and VEGF₁₂₀ isoforms and rat bFGF in the peri-infarct area of rat hearts post-myocardial infarction.

On page 14, please enter the amendment to the bridging paragraph of pages 13-14, beginning on line 29 of page 13, as follows:

Q3 In some embodiments, the invention provides methods for increasing or stimulating the expression of angiogenic cytokine production. Administration of an effective amount of a pharmaceutically active relaxin to an individual in need thereof increases angiogenic cytokine production by at least about 10%, at least about 20%, at least about 30%, at least about 50%, at least about 75%, at least about 100% (or two-fold), at least about 2.5-fold, at least about 3-fold, at least about 5-fold, or at least about 10-fold or more, compared to a suitable control. Angiogenic factors include, but are not limited to, fibroblast growth factor (FGF) FGF, including acidic FGF, basic FGF; VEGF, including VEGF-A, VEGF-B, VEGF-C, and synthetic and recombinant forms which possess VEGF activity, specifically angiogenic activity; hepatocyte growth factor (HGF); platelet-derived growth factor (PDGF); placental growth factor; angiopoietin-1; proliferin; insulin-like growth factor-1; granulocyte colony stimulating factor (G-CSF); transforming growth factor-α; and interleukin-8. Whether angiogenic cytokine production is increased following relaxin administration can be assessed using any method known in the art, including, but not limited to, measuring angiogenic cytokine levels using polymerase chain reaction (PCR) PCR, as described in Example 3; using an enzyme-linked immunosorbent assay (ELISA), or radioimmunoassay (RIA), using antibody specific for individual

angiogenic factors; and bioassays for specific individual angiogenic factors. See, e.g., Nicosia et al.

(1994) *Am. J. Pathol.* 145:1023-1029; Morishita et al. (1999) *Hypertension* 33: 1379-1384; Koblizek et al. (1998) *Curr. Biol.* 8:529-532; Schraufnagel et al. (1992) *J. Thorac. Cardiovasc. Surg.* 104:1582-

1588; and Yoshida et al. (1997) *Mol. Cell. Biol.* 17:4015-4023.

On page 25, please enter the amendment to the paragraph beginning on line 6, as follows:

Metabolic cage studies. Six rats were individually housed in Nalgene metabolism cages (Rodent Metabolism Cages for 150-300 g rats, VWR Scientific). Water and food were provided ad libidum. After 5-7 days of habituation, two baseline 24-hour urine collections were obtained. Then, an osmotic minipump containing purified porcine RLX was implanted (4 µg/hour). Additional 24-hour urine collections were made on days 2 and 5 of relaxin infusion and on days 4, 12, and 25 after exhaustion of the 7-day minipump. Food and water intake, as well as urinary flow rate were measured by gravimetric technique. The urinary excretion of sodium, cyclic guanosine monophosphate eGMP, and NO_x were also determined. The measurements made during the two baseline collections were averaged, as were the measurements made during the three post-relaxin collections.